Validation of contrast-enhanced magnetic resonance imaging to monitor regenerative efficacy after cell therapy in a porcine model of convalescent myocardial infarction.

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Public Summary:
Magnetic resonance imaging (MRI) in the CArdiosphere-Derived aUtologous stem CElls to reverse ventricULar dySfunction (CADUCEUS) trial revealed that cardiosphere-derived cells (CDCs) decrease scar size and increase viable myocardium after myocardial infarction (MI), but MRI has not been validated as an index of regeneration after cell therapy. We tested the validity of contrast-enhanced MRI in quantifying scarred and viable myocardium after cell therapy in a porcine model of convalescent MI.

Scientific Abstract:
BACKGROUND: Magnetic resonance imaging (MRI) in the CArdiosphere-Derived aUtologous stem CElls to reverse ventricULar dySfunction (CADUCEUS) trial revealed that cardiosphere-derived cells (CDCs) decrease scar size and increase viable myocardium after myocardial infarction (MI), but MRI has not been validated as an index of regeneration after cell therapy. We tested the validity of contrast-enhanced MRI in quantifying scarred and viable myocardium after cell therapy in a porcine model of convalescent MI. METHODS AND RESULTS: Yucatan minipigs underwent induction of MI and 2-3 weeks later were randomized to receive intracoronary infusion of 12.5x10(6) mismatched allogeneic CDCs or vehicle. Allogeneic CDCs induced mild local mononuclear infiltration but no systemic immunogenicity. MRI revealed that allogeneic CDCs attenuated remodeling, improved global and regional function, decreased scar size, and increased viable myocardium compared with placebo 2 months post-treatment. Extensive histological analysis validated quantitatively the MRI measurements of scar size, scar mass, and viable mass. CDCs neither altered gadolinium contrast myocardial kinetics nor induced changes in vascular density or architecture in viable and scarred myocardium. Histology demonstrated that CDCs lead to cardiomyocyte hyperplasia in the border zone, consistent with the observed stimulation of endogenous regenerative mechanisms (cardiomyocyte cycling, upregulation of endogenous progenitors, angiogenesis). CONCLUSIONS: Contrast-enhanced MRI accurately measures scarred and viable myocardium after cell therapy in a porcine model of convalescent MI. MRI represents a useful tool for assessing dynamic changes in the infarct and monitoring regenerative efficacy.